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APPLICATION NO	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO	CONFIRMATION NO.
09/601,371	12/05/2000	Tsukasa Seya	49927	2244

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EXAMINER
PRASAD, SARADA C

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 08/13/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/601,371	SEYA ET AL.	
	Examiner	Art Unit	
	Sarada C Prasad	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 June 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 3-5* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 3-5* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *13,14* .
4) ☒ Interview Summary (PTO-413) Paper No(s). *17* .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Detailed Action

1. Upon further consideration, the finality of the previous office action of Paper No. 12, (11/15/01) is withdrawn. It is noted that a notice of appeal has been filed. Applicant can request a refund for the associated fees or leave it as credit for future appeals.

As per applicants' request claims 2, and 6-10 have been cancelled, and amendments to claims 1, 3, and 5 have been entered. Currently, claims 1, 3-5 are under consideration for examination.

2. Applicant's arguments filed in Paper No. 16 (6/27/02), have been fully considered but were not deemed persuasive. The issues remaining and new issues, are stated below. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Specification

3. The information disclosure statement filed in Paper No. 14 (5/15/02) is objected to because the only cited reference in this disclosure is incomplete with neither disclosure of the Date, nor the Journal of Publication. Appropriate correction is required. Examiner acknowledges that the legible copy of the publication has been considered but lined through, and will not be printed upon issue unless a complete reference is supplied.

Claim Rejections - 35 USC § 101

4. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

4. Claims 1, 3-5 are rejected because the claimed invention is directed to non-statutory subject matter. Recitation of 'Cytokine inducers comprising M161Ag ...' in each of these claims reads on a product of nature, because M161Ag occurs in nature without the hand of man. Specification teaches that the M161Ag is a membrane protein which is present in cells infected with M. fermentans. This rejection can be obviated by amending the instant claims to recite 'An isolated or purified cytokine inducer comprising M161Ag.....' to introduce the hand of man.

Claim Rejections - 35 USC § 112-Second paragraph

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1, 3-5 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 and 5 are indefinite in recitation of 'gene recombination products...' because it is not clear what they are, and how are they related to SEQ ID No. 1 encoding the established M161Ag polypeptide(s). The metes and bounds of the instant limitation are not clear.

Claims objections:

Claims 3 and 4 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claims 3 and 4 do not further limit the product claimed in claim 1, because intended use does not limit or alter the product claimed.

Claim Rejections - 35 USC § 112-First paragraph

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Enablement:

6a. Rejection of claims 1, 3-5 under 35 USC 112 –first paragraph based on scope of enablement as set forth in earlier office actions of Paper No. 6 (3/14/01) and Paper No. 12 (11/15/01) is maintained, and is restated as follows.

Claims 1, 3-5 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for cytokine inducer comprising a lipoprotein Mycoplasma fermentans 161Ag having a polynucleotide sequence of SEQ ID No. 1, wherein the cytokines induced are selected form IL-6, IL-10, IL-12, TNF-α, IFN-γ, IL-1β, does not reasonably provide enablement for 'any other cytokine inducers' from M fermentans' or 'any other gene recombination products' or a method of use of cytokine inducers as 'immunomodulators'.

What the specification sets forth:

Given the teachings of the specification it is interpreted that the phrase 'cytokine inducers' encompasses several polypeptides derived from M. fermentans, these polypeptides are lipoproteins, SEQ ID No. 1 codes for one of them, several such additional polypeptides are present in the extracts of M. fermemtans. M161Ag induces cytokines such as IL-6, IL-10, IL-12, TNF-α, IFN-γ, IL-1β when incubated with peripheral blood monocytes.

The specification sets forth for a lipoprotein antigen identified as a polypeptide of SEQ ID No. 2 which stimulates monocytes to synthesize IL-6, IL-10, IL-12, TNF-α, IFN-γ, IL-1β.

However, the specification is not enabling for 'gene recombination products thereof' representing a genus of polypeptides, nor use of either as 'immunomodulators', nor such 'immunomodulators for remedy of diseases' that require immunomodulation.

Applicant's note of correction of M. fermentans as of bacterial origin and not of fungal origin is acknowledged. Also applicants' amendment to recite SEQ ID No. 1 in claim 1is acknowledged.

Analyses of Wands factors in support of the instant rejection of claims 1, 3-5:

What specification teaches: The specification and prior art teach a polynucleotide of SEQ ID No. 1 encoding the polypeptide of M161Ag. However, neither the specification nor prior art teach any other recombinant forms of M161Ag that retain the activities of M161Ag encoded by SEQ ID NO. 1. Teachings of Matsumato et al. include identification of three isoforms of M161Ag with amino acid changes (table 1, page 12413). However, neither the specification nor the citation of Matusmato et al. disclose if each of these three variants were equally active in producing cytokines, and which cytokines are induced in particular.

State of the art: Each of the cytokines induced by M161Ag possess distinct activities such as pro-inflammatory (TNF-α), and anti-inflammatory (IL-10). If M161Ag induces both of these cytokines, at the same time, it is not feasible for one of skill as to what type of immune-modulation should be expected.

Predictability in the art: Applicant argues that the cytokines induced by the M161Ag have known bioactivities, and these cytokines are useful in the treatment of diseases and therefore extrapolate that M161Ag which induces these cytokines in vitro would also serve an immunomodulatory role and be useful to treat disease and list examples such as (page 4, Paper

No. 16, 6/27/02). Applicants continue to support their argument by describing how each of the cytokines induced by M161Ag would be useful in supporting anti-viral activity (page 4, 2nd para –3rd para). However, these arguments have not been found to be persuasive, because the behavior of any specific, individual cytokines is not predictive that M161 Ag would function as an immunomodulator effective to remedy diseases given the number of different cytokines induced in vitro by M161 Ag. Therefore, one of skill in the art would not be able to plan a feasibility study of what cytokines would be needed to treat what immunological diseases.

Further, amendments to claims 3-5 do not obviate the instant rejection because the rejection is based on very broad claim language encompassing undisclosed potential of cytokines induced as remedies for treatment of 'any and all' immunological diseases.

Therefore, based on the above discussion, due to lack of guidance as to (a) what are the gene recombination products encompassed, (b) how to use these undescribed variants specifically, (c) treatment of which immunological diseases is to be addressed, and (d) what exactly is encompassed by recitation of immnomodulation other than induction of cytokines listed in claim 1, and unpredictability of what type of response to expect of a mixture of cytokines induced, one of skill would require undue experimentation to practice the instant claims. Therefore the rejection of record is maintained.

Written description

6b. Claims 1, 3-5 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants' assertions regarding the understanding of compliance with written description guidelines, and amendment to recite SEQ ID No. 1 in claim 1 are acknowledged. However, instant written description is not sufficient for recitation of "gene recombination products thereof" in the claim language without description of such variants of SEQ ID No. 1. Additionally, the specification fails to describe what are the many intended cytokine inducer polypeptides of claims 3-5.

The specification teaches induction of cytokines in monocytes by the lipoprotein antigen termed M161Ag derived from M fermentans. The disclosure also points to SEQ ID No. 1 as the polynucleotide encoding the polypeptide of SEQ ID No. 2. No other cytokine inducers comprising recombination products of M161Ag are disclosed. In light of this disclosure, there is no actual reduction to practice of realizing what are the expected gene recombination products, or methods of how to achieve them, or a clear depiction of such a genus. The specification has failed to describe what are the expected gene recombination products, what are the structural and functional characteristics, and convey that they are in possession of any such gene recombination products at the time of filing.

Weighting all the factors in view of the level of knowledge and skill in the art, one of skill would not recognize from the disclosure that the applicant was in possession of such gene recombination products that would encode for additional variants of M161Ag and induce cytokine synthesis in monocytes.

Applicants must convey with reasonable clarity, to those skilled in the art, as of the filing date sought, he or she was in possession of the invention. Therefore, mere contemplation of claimed cytokine inducers in the absence of adequate written description does not allow one

skilled in the art to envision the claimed invention. Conception of the claimed invention cannot be achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the potential methods for screening for the inhibitors. Therefore the Applicants have not provided sufficient evidence that they were in possession of the invention at the time of filing, as it is claimed, and thus written description requirement has not been satisfied for the claims as they are recited.

Applicant's attention is drawn to Guidelines for the examination of patent Applicants under 35 U.S.C. 112 first paragraph, "Written Description" requirement, federal register, Vol.66, No. pages 1099-111, Friday January, 2001.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

7a. Claims 1, 3-5 are rejected under 35 U.S.C. 102(b) as being anticipated by Matsumato et al. (1995, J Exp Med).

Matsumato et al. teach a membrane protein of 43 kDa identified by its antibody to be M161Ag (abstract, lines 8-9) which is identical to the protein M161Ag of the instant invention. Teachings of Matsumato et al. include that the M161Ag is also a potent activator of alternative complement pathway on human cells that activates homologous C3, and allows the deposition of C3b on itself (abstract, last 4 lines). Therefore, these teachings meet the limitations of instant

claims of the M161 Ag polypeptide with immunomodulatory activities, thus anticipating the instant claims 1, 3-5.

7b. Claims 1, 3-5 are rejected under 35 U.S.C. 102(a) as being anticipated by Matsumato et al. (1997, Nature Medicine).

Matsumato et al. teach a protein designated M161Ag, which was an unglycosylated 43-kDa protein with sequence identity to instant polypeptide encoded by SEQ ID No. 1. This protein bound to the surface of the cells and activated homologous complement (C3) via the alternative pathway (abstract, lines 10-end), thus disclosing its participation in immunomodulation. These teachings meet the limitations of instant claims 1, 3-5.

7c. Claims 1, 3-5 are rejected under 35 U.S.C. 102(a) as being anticipated by JP No. 9-157295 (June 1997).

JP No. 9-157295 discloses preparation of a probe for M161Ag for a membrane polypeptide termed M161Ag contained in the human myelocytic leukemia cell strain P39(+), its mRNA and cDNA (1.3 kbs) (base sequence in Fig. 2 and Fig. 3) (pages 5-6). JP No. 9-157295 also teaches proteins that would have substantially same amino acid sequence as this thus anticipating recombination products of the M161Ag and also demonstrate their C3 activating function (page 7). Instantly claimed immunomodulatory properties of the M161Ag polypeptide are inherent to the polypeptide itself, thus anticipating instant claims 1, 3-5.

7d. Claims 1, 3-5 are rejected under 35 U.S.C. 102(b) as being anticipated by Rawadi et al. (199).

Rawadi et al. isolate 'Heat Inactivated Mycoplasma fermentans' (HIM) particles that induce inflammatory cytokines such as IL-1, IL-6, TNF in monocytes (abstract, lines 3-4).

Rawadi's teachings also point out that this cytokine inducing activity of M fermentans membrane extracts consists of molecules that are associated with a lipid, and a protein fraction. Study of Rawadi et al. also includes that a cytotoxic activity is associated with the protein portion of the HIM particles. At the time the invention was made, Rawadi et al. did not identify such cytokine inducer activity as being due to M161Ag polypeptide, however their disclosure of such activity in mycoplasma membrane extracts active on myeloid cells meets the limitations of instant claims 1, 3-5.

Conclusion

8. No claims are allowed.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sarada C Prasad whose telephone number is 703-305-1009. The examiner can normally be reached Monday – Friday from 8.00 AM to 4.30 PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached on (703) 308-6564. The fax phone number for the organization where this application or proceeding is assigned is 703-308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Sarada Prasad, Ph.D.
Examiner
Art Unit 1646
July, 19th , 2002.

YVONNE EYLER, PH.D
SUPERVISORY PATENT EXAMINER
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